REMARKS

Receipt is acknowledged of the Final Office Action mailed September 23, 2003. Claims 23-25, 27-34, 37-40, 42-26, 50, 53, 54, 59 and 62-73 are pending. All the pending claims are herewith canceled in favor of new claims 71-92. No new matter is added with the new claims, which are fully supported by the specification. In the Annex, Applicants provide a listing of all the new claims with designations as to how they correspond to the old claims. Applicants provide new claims instead of amending the old claims for purposes of convenience.

I. Rejections under 35 USC § 112

In paragraphs 4 and 5, the Examiner rejects claims 23-25, 27-34, 42-46, 50, 53, 54, 59 and 62-70 under 35 USC § 112, first paragraph, for failing to satisfy the written description requirement. Specifically, the Examiner objected to the following phrase recited in claims 44 and 66: "The electrode structures are arranged so closely next to one another that they approach the size of large molecules." In response, applicants have cancelled the objected to claims and new claim 71 clarifies that the space between the electrodes approaches the size of a large molecule. This amendment is for clarification purposes and is fully supported in the specification, *inter alia* at page 3, lines 10-26. In view of this amendment, applicants respectfully request the Examiner to withdraw this rejection.

The Examiner also rejects claims 23-25, 27-34, 42-46, 50, 53-54, 59 and 62-70 for lack of enablement. Specifically, in paragraph 7, the Examiner questions whether the sample is desiccated. In response, applicants canceled claims 44 and 63 and new claim 71 indicates that the sample is a gel or a liquid. Accordingly, applicants request the Examiner to withdraw this rejection.

In paragraphs 9 and 10, the Examiner asserts that the specification fails to disclose reaction conditions and starting materials whereby any nucleic acid has been detected and is silent as to how any nucleic acid, protein or peptide is to be detected when it is part of a heterogeneous mixture. The Examiner also states that the specification is silent as to how one is to position the nucleic acid, protein or peptide by "chemical binding, adhesion, or condensation reaction" when the electrode is manufactured of any material, and not just the materials recited in claims 66-69.

In response, applicants point out that new claim 71 clearly recites a method by which a first molecule or molecular complex binds a second molecule that is bound to the surface of the microelectrode structure. This addresses the Examiner's concern about the heterogeneity of the sample and how the molecule to be detected is positioned. Claim 71 also recites that the electrode structures comprise a "conductive material" to respond to the Examiner's concern that the electrode of the invention is made out of "any material."

In paragraph 11, the Examiner rejects claims 24 and 27 as being objectionable for a variety of reasons. In response, applicants have canceled claims 24 and 27.

In paragraph 20, the Examiner rejects claims 23-25, 27-34, 37-40, 42-46, 50, 53-54, 59 and 62-70 for lack of enablement, stated that the specification fails to overcome art-recognized difficulties as set forth in U.S. Patent No. 6,391,624. Specifically, the Examiner states that the specification is effectively silent as to how low concentrations of nucleic acid, polypeptides or peptides are to be detected. The Examiner's concern about the low concentration of the molecule to be detected appears to be related to his concern about the heterogeneity of the sample. That is, how is a molecule going to be positioned in such a way as to be detected? Applicants believe that new claim 71 clarifies how a molecule can be detected via binding another molecule that is bound to the electrode. The specification clearly supports this invention at page 7, lines 20-21 (second molecule bound to microelectrode structures) and page 9, line 15 to page 10, line 2 (bonding groups on bound molecule).

In paragraph 22, the examiner rejects claims 23-25, 27-34, 37-40, 42-46, 50, 53-54, 59 and 62-70 under 35 USC § 112, second paragraph. Specifically, the Examiner questions the "metes and bounds" of "large molecular complexes." Applicants respond that one of skill in the art would understand that large molecular complexes are proteins or DNA complexes.

In paragraphs 24 and 25, the Examiner objects to "impedance spectroscopy recited in claim 23. In response, applicants have canceled claim 23.

In view of the above new claims and explanations, applicants respectfully request the Examiner to withdraw all rejections under 35 USC § 112.

II. Rejections under 35 USC § 101

The Examiner has rejected claims 23-25, 27-34, 37-40, 42-46, 50, 53-54, 59 and 62-70 under 35 USC §101 for lack of operability. The Examiner questions how the electrode structures could be reduced in size to where the overall structure approaches the size of large molecule complexes. Applicants explain that new claims 71 clarifies that it is the space between the electrodes that approaches the size of large molecule complexes.

In view of new claim 71, applicants respectfully request the examiner to withdraw the rejection under 35 USC § 101.

III. Rejections under 35 USC § 103

Applicants acknowledge the Examiner's withdrawal of previous obviousness rejections.

CONCLUSION

Applicants respectfully request Examiner Sisson to consider the above remarks and enter the new claims, which applicants assert are in condition for allowance. Early notification of allowance is earnestly requested. Examiner Sisson is encouraged to contact the undersigned

attorney for applicants at 202-912-2142 for any reason related to the advancement of this case.

Respectfully submitted,

Date: March 22, 2004

Patricia D. Granados
Attorney for Applicant
Reg. No.: 33,683

Heller Ehrman White & McAuliffe LLP
1666 K Street, N.W., Suite 300
Washington, D.C. 20006-4004
Telephone: (202) 912-2000
Facsimile: (202) 912-2020

Customer No. 26633

ANNEX

This Annex shows the correspondence of the new claims to the previous set of claims, for the examiner's convenience.

71. (Amended claim 63) A method of detecting a first molecule or a first molecular complex in a liquid or gel, comprising:

(a) providing a single ultra-microelectrode array, said ultra-microelectrode array comprising at least two electrode structures, wherein a second molecule is bound to the surface of the microelectrode structures and comprises a bonding group that can bind the first molecule by a chemical reaction or by complexing, the second molecule being capable of binding to a first molecule or molecular complex to be detected,

(b) contacting the first molecule or a first molecular complex in the liquid or gel with the ultra-microelectrode array;

(c) producing an electric field between the electrode structures;

(d) measuring changes in current or potential between the electrode structures, whereby the changes in current or potential are caused by the first molecule or the first molecular complex that binds to the second molecule; and

(e) detecting the presence of said first molecule or first molecular complex by observing said change in current or potential;

wherein said first molecule or first molecular complex is selected from the group consisting of nucleic acids, peptides and proteins; and

wherein each of said electrode structures comprises a surface layer

of conductive material, is insulated from each other and is either a layer on a planar insulating support material, or is incorporated in said planar insulating support material and wherein the space between the electrode structures is about 1 µm or less to approaching the size of a large molecule complex.

72. (Previously presented claim 64) The method according to claim 71, wherein the second molecule is positioned on an electrode or to a surface of a gap between electrodes by chemical binding, adhesion, or condensation reaction.

73. (Previously presented claim 23) The method according to claim 71, wherein the measuring of the changes in current or potential is performed using impedance spectroscopy.

74. (Previously presented claim 31) The method according to claim 71, wherein the second molecule is bound via a binding compound on the surface of the electrode structures.

75. (Amended claim 32) The method according to claim 71, wherein the second molecule binds to the surface of the electrode structures via physical or chemical binding. or is bound via a binding compound.

76. (Amended claim 33) The method according to claim 71, wherein the second molecule binds to surface of the electrode structures via self-assembling.

77. (Amended claim 34) The method according to claim, 74 wherein the second molecule is bound to the binding compound on the surface of the electrode structures-via electropolymerization.

78. (Amended claim 65) The method according to claim 71, wherein said second molecule comprises an antibody, and wherein the first molecule or first molecular complex to be detected comprises an antigen that binds to said antibody.

79. (Amended claim 38) The method according to claim 71, wherein the second molecule binds the binding compound on a surface of the electrode structures.

80. (Amended claim 39) The method according to claim 71, wherein the second molecule comprises biotin.

81. (Amended claim 40) The method according to claim 71, wherein the second molecule comprises an antigen, and wherein the first molecule or first molecular complex to be detected comprises an antibody.

82. (Previously presented claim 42) The method according to claim 71, wherein the second molecule comprises a first polynucleotide, and the first molecule or first molecular complex to be detected comprises a second polynucleotide capable of binding to the first polynucleotide.

83. (Previously presented claim 43) The method according to claim 82, wherein the second polynucleotide binds to the first polynucleotide via hybridization.

84. (Amended claim 44) A method according to claim 71, wherein said first molecule or molecular complex is a third polynucleotide that hybridizes to the second molecule which is a second polynucleotide that is hybridized to a first polynucleotide, wherein said first polynucleotide is bound to a binding compound on said ultra-microelectrode array.

85. (Previously presented claim 50) The method according to claim 71, wherein the insulating material is selected from the group consisting of silicon compounds, glass, ceramic and organic polymers.

86. (Previously presented claim 53) The method according to claim 71, wherein the insulating material is selected from the group consisting of silicon oxides, nitrides, and plastics.

87. (Previously presented claim 54) The method according to claim 71, wherein the electrode structures are arranged as a multi-layer structure with each layer insulated from the others.

88. (Amended claim 59) The method according to claim 71, wherein the changes in current or potential are measured sequentially, in parallel or simultaneously.

89. (Amended claim 66) The method of claim 71, wherein said layer of conductive material is selected from the group consisting of a noble metal, a carbon material and both a noble metal and carbon material.

90. (Amended claim 68) The method of claim 89, wherein said noble metal is selected from the group consisting of gold, platinum and iridium.

91. (Amended claim 70) The method according to claim 71 wherein each of the electrode structures is a layer sufficiently thin that the ultra-microelectrode array is substantially planar.

92. (New) A method according to claim 87, wherein the multilayer electrode structures are stacked, and comprise crossover points that are insulated from one another.